CAS ONLINE PRINTOUT 09/698,071

=> d his

(FILE 'HOME' ENTERED AT 07:20:14 ON 11 SEP 2002)

FILE 'REGISTRY' ENTERED AT 07:20:37 ON 11 SEP 2002
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L2 1 S L1
L3 56 S L1 FUL
L4 STRUCTURE UPLOADED
L5 0 S L4
L6 13 SEARCH L4 SSS SUB=L3 FULL

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L7 8 S L6

FILE 'REGISTRY' ENTERED AT 07:37:28 ON 11 SEP 2002
L8 STRUCTURE UPLOADED
L9 6 SEARCH L8 SSS SUB=L3 FULL

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L10 4 S L9

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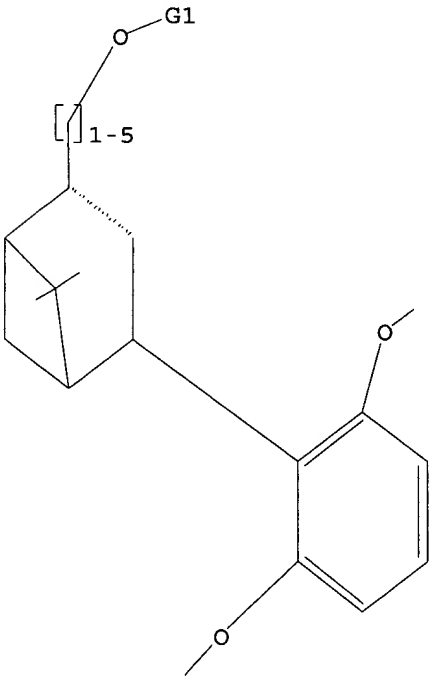
L8 HAS NO ANSWERS
L8 STR



G1 Me,Et,n-Pr,i-Pr,H

Structure attributes must be viewed using STN Express query preparation.

=> d bib abs hitstr 1-4

L10 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2002 ACS
AN 2001:338346 CAPLUS
DN 134:348297

CAS ONLINE PRINTOUT 09/698,071

TI 4-Phenyl pinene derivatives as agonists specific for the peripheral cannabinoid receptor and their therapeutic uses

IN Fride, Ester; Breuer, Aviva; Hanus, Lumir; Tchilibon, Susanna; Horowitz, Michal; Mechoulam, Raphael; Garzon, Aaron

PA Yissum Research Development Company of the Hebrew University, Israel

SO PCT Int. Appl., 43 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001032169	A1	20010510	WO 2000-US29903	20001030

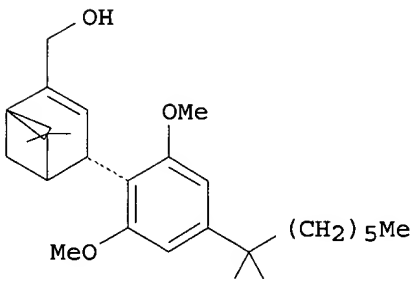
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI IL 1999-132661 A 19991031

OS MARPAT 134:348297

GI



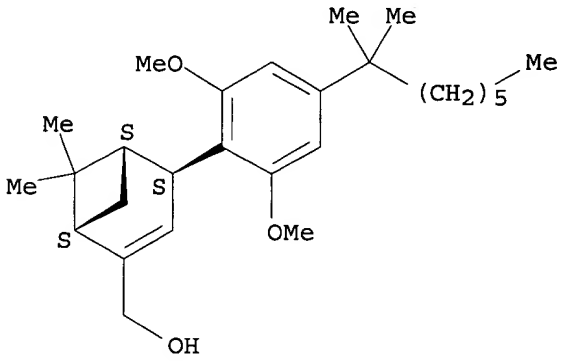
I

AB The invention provides novel pharmaceutical compns. comprising as the active ingredient 4-Ph pinene derivs. which are specific for the peripheral cannabinoid receptors. In particular, the compds. of the invention bind efficiently to CB2 but do not bind to CB1. The compds. show no activity in behavioral tests in mice which together have been shown to be specific for tetrahydrocannabinol (THC)- type activity in the central nervous system mediated by CB1 but reduce blood pressure, block intestinal mobility, and elicit anti-inflammatory and peripheral analgetic activity. The invention also relates to methods of treating, preventing, or managing hypertension, inflammation, pain, gastrointestinal diseases, autoimmune diseases, and tumors with the compds. of the invention. HU-308 (I) (prepn. given) at 10 and 20 mg/kg, administer i.p. to mice daily for seven days, reduced the severity of acid-induced inflammatory bowel disease.

IT **256934-39-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(4-Ph pinene derivs. as agonists specific for peripheral cannabinoid

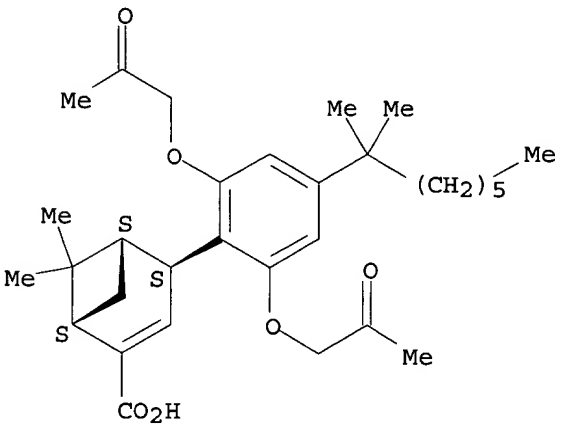
receptor and therapeutic uses)
RN 256934-39-1 CAPLUS
CN Bicyclo[3.1.1]hept-2-ene-2-methanol, 4-[4-(1,1-dimethylheptyl)-2,6-dimethoxyphenyl]-6,6-dimethyl-, (1R,4R,5R)-rel-(+)- (9CI) (CA INDEX NAME)

Rotation (+). Absolute stereochemistry unknown.



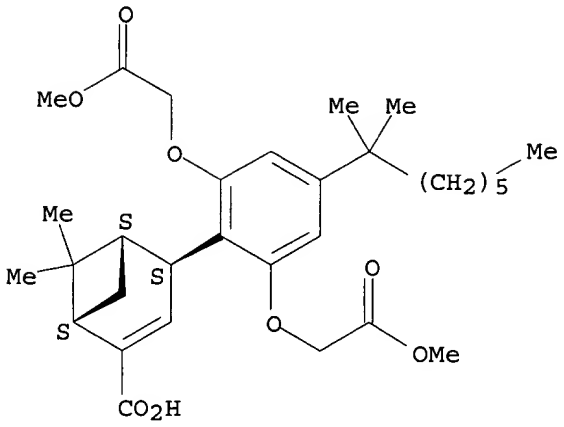
IT **338971-67-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(4-Ph pinene derivs. as agonists specific for peripheral cannabinoid receptor and therapeutic uses)
RN 338971-67-8 CAPLUS
CN Bicyclo[3.1.1]hept-2-ene-2-carboxylic acid, 4-[4-(1,1-dimethylheptyl)-2,6-bis(2-oxopropoxy)phenyl]-6,6-dimethyl-, (1R,4R,5R)-rel-(+)- (9CI) (CA INDEX NAME)

Rotation (+). Absolute stereochemistry unknown.



IT **338971-68-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(4-Ph pinene derivs. as agonists specific for peripheral cannabinoid receptor and therapeutic uses)
RN 338971-68-9 CAPLUS
CN Bicyclo[3.1.1]hept-2-ene-2-carboxylic acid, 4-[4-(1,1-dimethylheptyl)-2,6-bis(2-methoxy-2-oxoethoxy)phenyl]-6,6-dimethyl-, (1R,4R,5R)-rel-(+)- (9CI) (CA INDEX NAME)

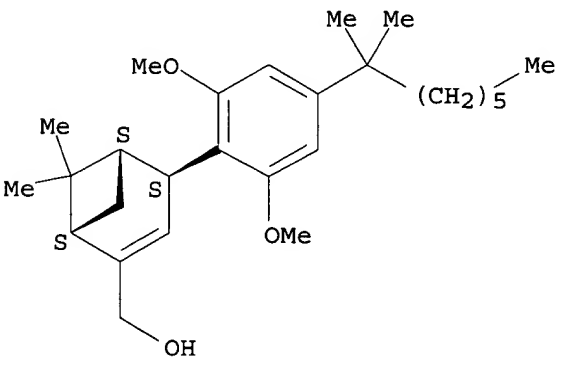
Rotation (+). Absolute stereochemistry unknown.



RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2002 ACS
AN 2000:614228 CAPLUS
DN 133:260976
TI Looking back at cannabis research
AU Mechoulam, Raphael
CS Medical Faculty, Department of Medicinal Chemistry and Natural Products, Hebrew University, Jerusalem, 91120, Israel
SO Current Pharmaceutical Design (2000), 6(13), 1313-1322
CODEN: CPDEFP; ISSN: 1381-6128
PB Bentham Science Publishers
DT Journal; General Review
LA English
AB A review with 70 refs. Research leading to the isolation of the plant cannabinoids during the 1960's and to the endogenous cannabinoids, during the 1990's is described. Investigations on two non-psychotropic, synthetic cannabinoids, HU-211, a neuroprotective agent and HU-308, a specific CB2 agonist are presented.
IT **256934-39-1**, HU 308
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(looking back at cannabis research)
RN 256934-39-1 CAPLUS
CN Bicyclo[3.1.1]hept-2-ene-2-methanol, 4-[4-(1,1-dimethylheptyl)-2,6-dimethoxyphenyl]-6,6-dimethyl-, (1R,4R,5R)-rel-(+)- (9CI) (CA INDEX NAME)

Rotation (+). Absolute stereochemistry unknown.

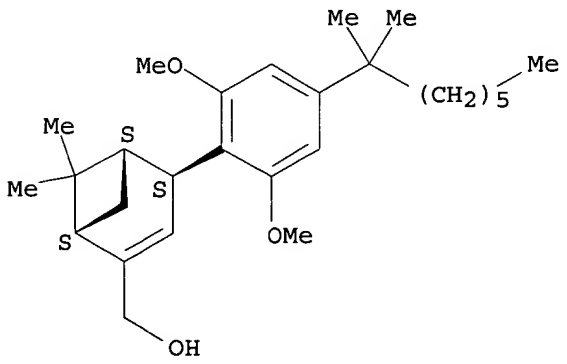


CAS ONLINE PRINTOUT 09/698,071

RE.CNT 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2002 ACS
AN 1999:796665 CAPLUS
DN 132:132238
TI HU-308: a specific agonist for CB2, a peripheral cannabinoid receptor
AU Hanus, L.; Breuer, A.; Tchilibon, S.; Shiloah, S.; Goldenberg, D.; Horowitz, M.; Pertwee, R. G.; Ross, R. A.; Mechoulam, R.; Fride, E.
CS Department of Medicinal Chemistry and Natural Products, Medical Faculty, Hebrew University, Jerusalem, 91120, Israel
SO Proceedings of the National Academy of Sciences of the United States of America (1999), 96(25), 14228-14233
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
AB Two cannabinoid receptors have been identified: CB1, present in the central nervous system (CNS) and to a lesser extent in other tissues, and CB2, present outside the CNS, in peripheral organs. There is evidence for the presence of CB2-like receptors in peripheral nerve terminals. We report now that we have synthesized a CB2-specific agonist, code-named HU-308. This cannabinoid does not bind to CB1 (Ki > 10 .mu.M), but does so efficiently to CB2 (Ki = 22.7 .+-. 3.9 nM); it inhibits forskolin-stimulated cAMP prodn. in CB2-transfected cells, but does so much less in CB1-transfected cells. HU-308 shows no activity in mice in a tetrad of behavioral tests, which together have been shown to be specific for tetrahydrocannabinol (THC)-type activity in the CNS mediated by CB1. However, HU-308 reduces blood pressure, blocks defecation, and elicits anti-inflammatory and peripheral analgesic activity. The hypotension, the inhibition of defecation, the anti-inflammatory and peripheral analgesic effects produced by HU-308 are blocked (or partially blocked) by the CB2 antagonist SR-144528, but not by the CB1 antagonist SR-141716A. These results demonstrate the feasibility of discovering novel nonpsychotropic cannabinoids that may lead to new therapies for hypertension, inflammation, and pain.
IT **256934-39-1P**, HU 308
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(HU-308: a specific agonist for CB2, a peripheral cannabinoid receptor)
RN 256934-39-1 CAPLUS
CN Bicyclo[3.1.1]hept-2-ene-2-methanol, 4-[4-(1,1-dimethylheptyl)-2,6-dimethoxyphenyl]-6,6-dimethyl-, (1R,4R,5R)-rel-(+)- (9CI) (CA INDEX NAME)

Rotation (+). Absolute stereochemistry unknown.



CAS ONLINE PRINTOUT 09/698,071

RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2002 ACS
AN 1995:759141 CAPLUS
DN 123:314212
TI Preparation and neuroprotective pharmaceutical compositions of 4-phenylpinene derivatives
IN Mechoulam, Raphael; Breuer, Aviva; Biegon, Anat
PA Yissum Research Development Co., USA; Pharmos Corp.
SO U.S., 24 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5434295	A	19950718	US 1994-192924	19940207
	IL 112558	A1	20000726	IL 1995-112558	19950206
PRAI	US 1994-192924	A	19940207		

OS MARPAT 123:314212
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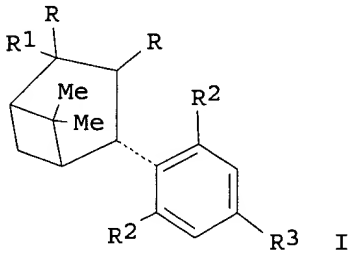

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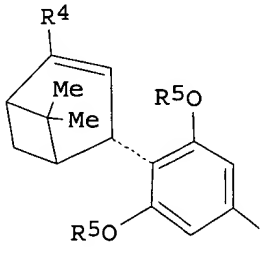


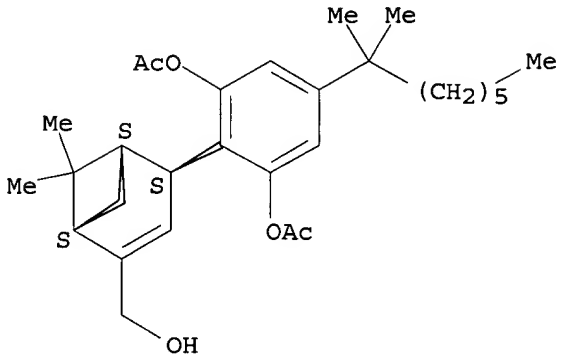
II

AB The title compds. I (R = H, R2 = bond; R1 = a variety of org. moieties; R2 = alkyl, halo, various oxy groups; R3 = alkyl groups, ether groups, or combinations thereof) were prepd. as active ingredients of pharmaceutical compns. displaying neuroprotectant and antiglaucoma effects. Thus, 4-hydroxymyrtenyl pivalate was treated with 5-(1,1-dimethylheptyl)resorcinol to give the title deriv. II (R4 = CH2O2CCMe3, R5 = H), which was converted to II (R = CO2H, R1 = Ac) (III) in several steps. At 1 .mu.M III blocked the NMDA response at the glutamate receptor by 35%. III caused a significant redn. in intraocular pressure in rabbits which indicated a possible therapeutic use in glaucoma treatment.

IT **169287-91-6P 169287-93-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and neuroprotective pharmaceutical compns. of 4-phenylpinene derivs.)

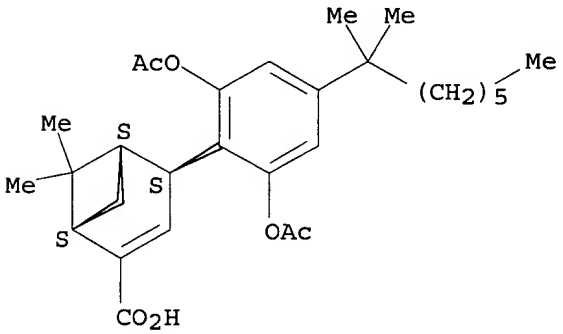
RN 169287-91-6 CAPLUS
CN 1,3-Benzenediol, 5-(1,1-dimethylheptyl)-2-[4-(hydroxymethyl)-6,6-dimethylbicyclo[3.1.1]hept-3-en-2-yl]-, 1,3-diacetate, [1S-(1.alpha.,2.alpha.,5.alpha.)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 169287-93-8 CAPLUS
CN Bicyclo[3.1.1]hept-2-ene-2-carboxylic acid, 4-[2,6-bis(acetyloxy)-4-(1,1-dimethylheptyl)phenyl]-6,6-dimethyl-, [1S-(1.alpha.,4.alpha.,5.alpha.)]- (9CI) (CA INDEX NAME)

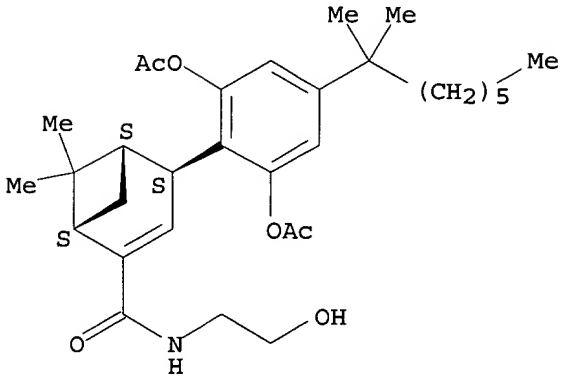
Absolute stereochemistry. Rotation (+).



IT **169287-98-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and neuroprotective pharmaceutical compns. of 4-phenylpinene derivs.)
RN 169287-98-3 CAPLUS
CN Bicyclo[3.1.1]hept-2-ene-2-carboxamide, 4-[2,6-bis(acetyloxy)-4-(1,1-dimethylheptyl)phenyl]-N-(2-hydroxyethyl)-6,6-dimethyl-, [1S-(1.alpha.,4.alpha.,5.alpha.)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

CAS ONLINE PRINTOUT 09/698,071



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CAS ONLINE PRINTOUT 09/698,071

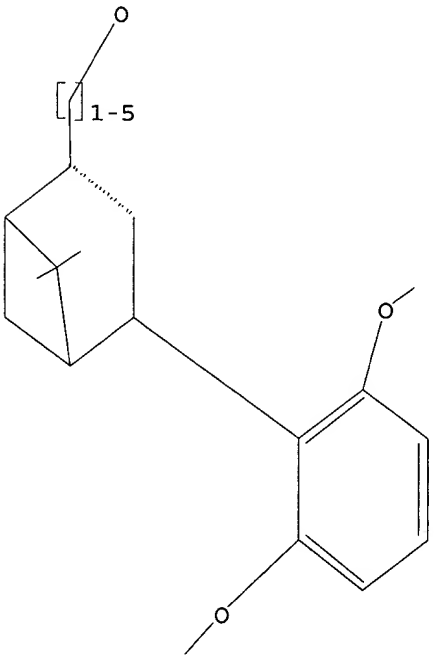
=> d his

(FILE 'HOME' ENTERED AT 07:20:14 ON 11 SEP 2002)

FILE 'REGISTRY' ENTERED AT 07:20:37 ON 11 SEP 2002
L1 STRUCTURE UPLOADED
L2 1 S L1
L3 56 S L1 FUL
L4 STRUCTURE UPLOADED
L5 0 S L4
L6 13 SEARCH L4 SSS SUB=L3 FULL

FILE 'CAPLUS' ENTERED AT 07:23:53 ON 11 SEP 2002
L7 8 S L6

=> d l4
L4 HAS NO ANSWERS
L4 STR



Structure attributes must be viewed using STN Express query preparation.

=> d bib abs hitstr 1-8

L7 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2002 ACS
AN 2001:338346 CAPLUS
DN 134:348297
TI 4-Phenyl pinene derivatives as agonists specific for the peripheral cannabinoid receptor and their therapeutic uses
IN Fride, Ester; Breuer, Aviva; Hanus, Lumir; Tchilibon, Susanna; Horowitz, Michal; Mechoulam, Raphael; Garzon, Aaron
PA Yissum Research Development Company of the Hebrew University, Israel
SO PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DT Patent
LA English

CAS ONLINE PRINTOUT 09/698,071

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001032169	A1	20010510	WO 2000-US29903	20001030

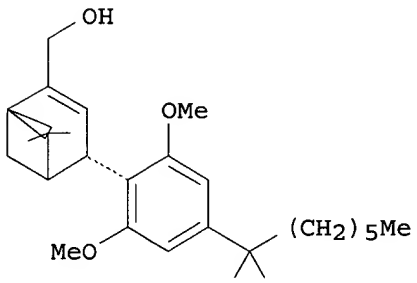
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI IL 1999-132661 A 19991031

OS MARPAT 134:348297

GI



I

AB The invention provides novel pharmaceutical compns. comprising as the active ingredient 4-Ph pinene derivs. which are specific for the peripheral cannabinoid receptors. In particular, the compds. of the invention bind efficiently to CB2 but do not bind to CB1. The compds. show no activity in behavioral tests in mice which together have been shown to be specific for tetrahydrocannabinol (THC)- type activity in the central nervous system mediated by CB1 but reduce blood pressure, block intestinal mobility, and elicit anti-inflammatory and peripheral analgetic activity. The invention also relates to methods of treating, preventing, or managing hypertension, inflammation, pain, gastrointestinal diseases, autoimmune diseases, and tumors with the compds. of the invention. HU-308 (I) (prepn. given) at 10 and 20 mg/kg, administer i.p. to mice daily for seven days, reduced the severity of acid-induced inflammatory bowel disease.

IT **256934-39-1P**

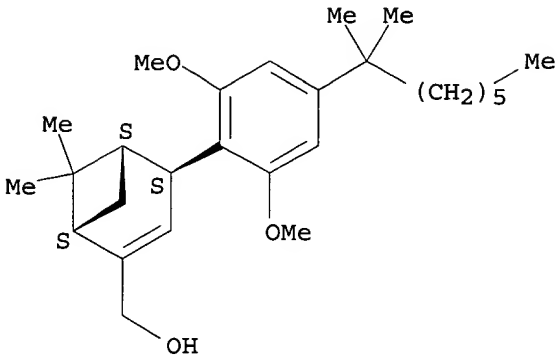
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(4-Ph pinene derivs. as agonists specific for peripheral cannabinoid receptor and therapeutic uses)

RN 256934-39-1 CAPLUS

CN Bicyclo[3.1.1]hept-2-ene-2-methanol, 4-[4-(1,1-dimethylheptyl)-2,6-dimethoxyphenyl]-6,6-dimethyl-, (1R,4R,5R)-rel-(+)- (9CI) (CA INDEX NAME)

Rotation (+). Absolute stereochemistry unknown.

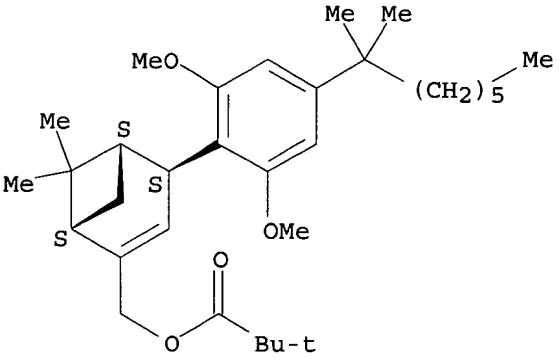


IT **256665-46-0P 338971-67-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(4-Ph pinene derivs. as agonists specific for peripheral cannabinoid receptor and therapeutic uses)

RN 256665-46-0 CAPLUS

CN Propanoic acid, 2,2-dimethyl-, [(1R,4R,5R)-4-[4-(1,1-dimethylheptyl)-2,6-dimethoxyphenyl]-6,6-dimethylbicyclo[3.1.1]hept-2-en-2-yl]methyl ester, rel- (9CI) (CA INDEX NAME)

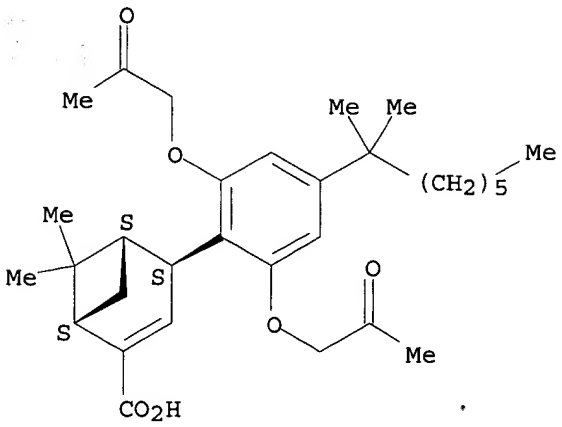
Relative stereochemistry.



RN 338971-67-8 CAPLUS

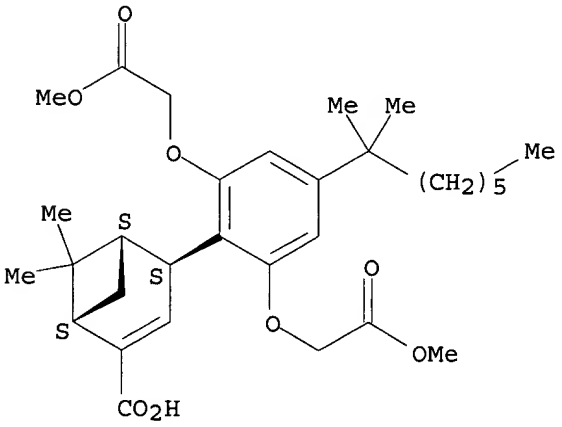
CN Bicyclo[3.1.1]hept-2-ene-2-carboxylic acid, 4-[4-(1,1-dimethylheptyl)-2,6-bis(2-oxopropoxy)phenyl]-6,6-dimethyl-, (1R,4R,5R)-rel-(+)- (9CI) (CA INDEX NAME)

Rotation (+). Absolute stereochemistry unknown.



IT **338971-68-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(4-Ph pinene derivs. as agonists specific for peripheral cannabinoid receptor and therapeutic uses)
RN 338971-68-9 CAPLUS
CN Bicyclo[3.1.1]hept-2-ene-2-carboxylic acid, 4-[4-(1,1-dimethylheptyl)-2,6-bis(2-methoxy-2-oxoethoxy)phenyl]-6,6-dimethyl-, (1R,4R,5R)-rel-(+)- (9CI) (CA INDEX NAME)

Rotation (+). Absolute stereochemistry unknown.



RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2002 ACS
AN 2000:614228 CAPLUS
DN 133:260976
TI Looking back at cannabis research
AU Mechoulam, Raphael
CS Medical Faculty, Department of Medicinal Chemistry and Natural Products, Hebrew University, Jerusalem, 91120, Israel
SO Current Pharmaceutical Design (2000), 6(13), 1313-1322
CODEN: CPDEFP; ISSN: 1381-6128
PB Bentham Science Publishers
DT Journal; General Review
LA English
AB A review with 70 refs. Research leading to the isolation of the plant cannabinoids during the 1960's and to the endogenous cannabinoids, during

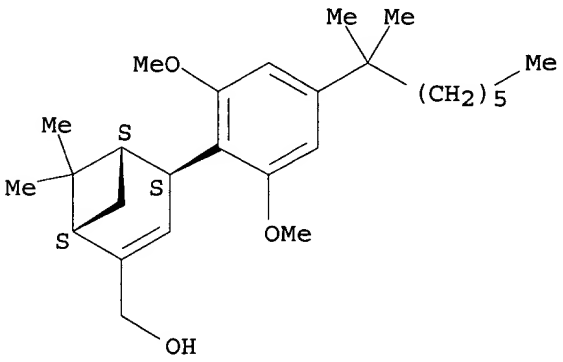
the 1990's is described. Investigations on two non-psychotropic, synthetic cannabinoids, HU-211, a neuroprotective agent and HU-308, a specific CB2 agonist are presented.

IT **256934-39-1**, HU 308
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(looking back at cannabis research)

RN 256934-39-1 CAPLUS

CN Bicyclo[3.1.1]hept-2-ene-2-methanol, 4-[4-(1,1-dimethylheptyl)-2,6-dimethoxyphenyl]-6,6-dimethyl-, (1R,4R,5R)-rel-(+)- (9CI) (CA INDEX NAME)

Rotation (+). Absolute stereochemistry unknown.



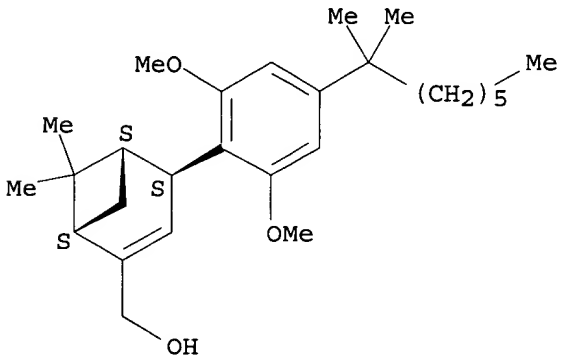
RE.CNT 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2002 ACS
AN 1999:796665 CAPLUS
DN 132:132238
TI HU-308: a specific agonist for CB2, a peripheral cannabinoid receptor
AU Hanus, L.; Breuer, A.; Tchilibon, S.; Shiloah, S.; Goldenberg, D.; Horowitz, M.; Pertwee, R. G.; Ross, R. A.; Mechoulam, R.; Fride, E.
CS Department of Medicinal Chemistry and Natural Products, Medical Faculty, Hebrew University, Jerusalem, 91120, Israel
SO Proceedings of the National Academy of Sciences of the United States of America (1999), 96(25), 14228-14233
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
AB Two cannabinoid receptors have been identified: CB1, present in the central nervous system (CNS) and to a lesser extent in other tissues, and CB2, present outside the CNS, in peripheral organs. There is evidence for the presence of CB2-like receptors in peripheral nerve terminals. We report now that we have synthesized a CB2-specific agonist, code-named HU-308. This cannabinoid does not bind to CB1 (Ki > 10 .mu.M), but does so efficiently to CB2 (Ki = 22.7 .+-. 3.9 nM); it inhibits forskolin-stimulated cAMP prodn. in CB2-transfected cells, but does so much less in CB1-transfected cells. HU-308 shows no activity in mice in a tetrad of behavioral tests, which together have been shown to be specific for tetrahydrocannabinol (THC)-type activity in the CNS mediated by CB1. However, HU-308 reduces blood pressure, blocks defecation, and elicits anti-inflammatory and peripheral analgesic activity. The hypotension, the inhibition of defecation, the anti-inflammatory and peripheral analgesic effects produced by HU-308 are blocked (or partially blocked) by the CB2 antagonist SR-144528, but not by the CB1 antagonist SR-141716A. These results demonstrate the feasibility of discovering novel nonpsychotropic

cannabinoids that may lead to new therapies for hypertension, inflammation, and pain.

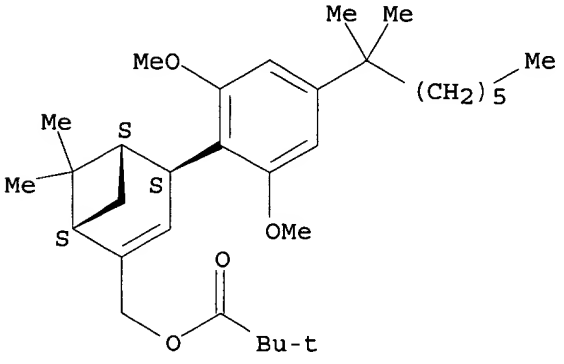
IT **256934-39-1P**, HU 308
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(HU-308: a specific agonist for CB2, a peripheral cannabinoid receptor)
RN 256934-39-1 CAPLUS
CN Bicyclo[3.1.1]hept-2-ene-2-methanol, 4-[4-(1,1-dimethylheptyl)-2,6-dimethoxyphenyl]-6,6-dimethyl-, (1R,4R,5R)-rel-(+)- (9CI) (CA INDEX NAME)

Rotation (+). Absolute stereochemistry unknown.



IT **256665-46-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(HU-308: a specific agonist for CB2, a peripheral cannabinoid receptor)
RN 256665-46-0 CAPLUS
CN Propanoic acid, 2,2-dimethyl-, [(1R,4R,5R)-4-[4-(1,1-dimethylheptyl)-2,6-dimethoxyphenyl]-6,6-dimethylbicyclo[3.1.1]hept-2-en-2-yl]methyl ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2002 ACS
AN 1995:759141 CAPLUS
DN 123:314212
TI Preparation and neuroprotective pharmaceutical compositions of

CAS ONLINE PRINTOUT 09/698,071

4-phenylpinene derivatives

IN Mechoulam, Raphael; Breuer, Aviva; Biegon, Anat

PA Yissum Research Development Co., USA; Pharmos Corp.

SO U.S., 24 pp.
CODEN: USXXAM

DT Patent

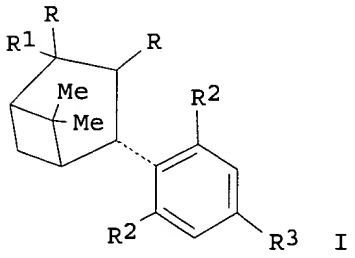
LA English

FAN.CNT 1

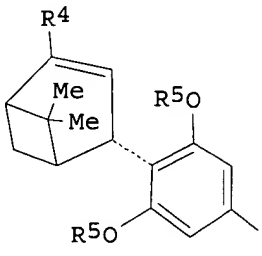
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5434295	A	19950718	US 1994-192924	19940207
	IL 112558	A1	20000726	IL 1995-112558	19950206
PRAI	US 1994-192924	A	19940207		

OS MARPAT 123:314212

GI



I



II

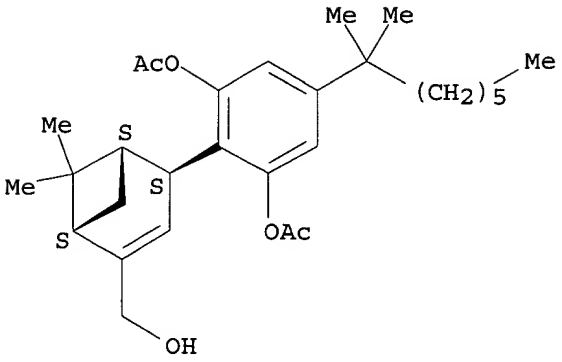
AB The title compds. I (R = H, R2 = bond; R1 = a variety of org. moieties; R2 = alkyl, halo, various oxy groups; R3 = alkyl groups, ether groups, or combinations thereof) were prepd. as active ingredients of pharmaceutical compns. displaying neuroprotectant and antiglaucoma effects. Thus, 4-hydroxymyrtenyl pivalate was treated with 5-(1,1-dimethylheptyl)resorcinol to give the title deriv. II (R4 = CH2O2CCMe3, R5 = H), which was converted to II (R = CO2H, R1 = Ac) (III) in several steps. At 1 .mu.M III blocked the NMDA response at the glutamate receptor by 35%. III caused a significant redn. in intraocular pressure in rabbits which indicated a possible therapeutic use in glaucoma treatment.

IT **169287-91-6P 169287-93-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and neuroprotective pharmaceutical compns. of 4-phenylpinene derivs.)

RN 169287-91-6 CAPLUS

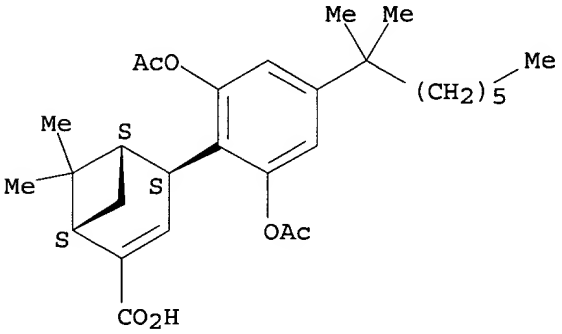
CN 1,3-Benzenediol, 5-(1,1-dimethylheptyl)-2-[4-(hydroxymethyl)-6,6-dimethylbicyclo[3.1.1]hept-3-en-2-yl]-, 1,3-diacetate, [1S-(1.alpha.,2.alpha.,5.alpha.)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

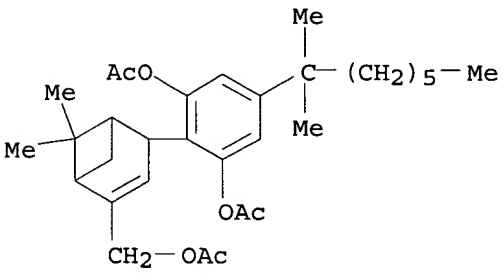


RN 169287-93-8 CAPLUS
CN Bicyclo[3.1.1]hept-2-ene-2-carboxylic acid, 4-[2,6-bis(acetyloxy)-4-(1,1-dimethylheptyl)phenyl]-6,6-dimethyl-, [1S-(1.alpha.,4.alpha.,5.alpha.)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



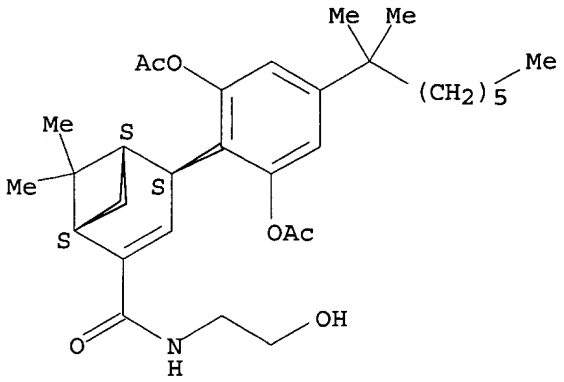
IT **76163-87-6P**, HU 254 **169287-98-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and neuroprotective pharmaceutical compns. of 4-phenylpinene derivs.)
RN 76163-87-6 CAPLUS
CN 1,3-Benzenediol, 2-[4-[(acetyloxy)methyl]-6,6-dimethylbicyclo[3.1.1]hept-3-en-2-yl]-5-(1,1-dimethylheptyl)-, diacetate, [1S-(1.alpha.,2.alpha.,5.alpha.)]- (9CI) (CA INDEX NAME)



RN 169287-98-3 CAPLUS
CN Bicyclo[3.1.1]hept-2-ene-2-carboxamide, 4-[2,6-bis(acetyloxy)-4-(1,1-

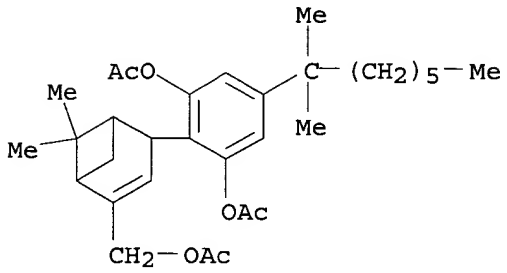
dimethylheptyl)phenyl]-N-(2-hydroxyethyl)-6,6-dimethyl-, [1S-(1.alpha.,4.alpha.,5.alpha.)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

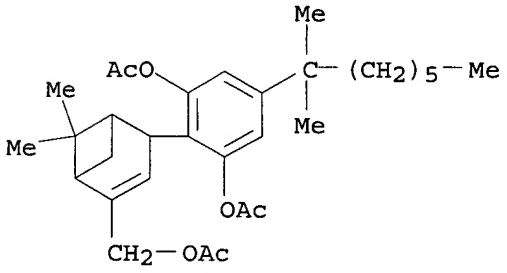


L7 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2002 ACS
AN 1993:246926 CAPLUS
DN 118:246926
TI Discriminative stimulus effects and receptor binding of enantiomeric pairs of cannabinoids in rats and pigeons; a comparison
AU Jaerbe, Torbjoern U. C.; Hiltunen, Arto J.; Mathis, Diane A.; Hanus, Lumir; Breuer, Aviva; Mechoulam, Raphael
CS Fac. Soc. Sci., Univ. Uppsala, Uppsala, S-751 48, Swed.
SO J. Pharmacol. Exp. Ther. (1993), 264(2), 561-9
CODEN: JPETAB; ISSN: 0022-3565
DT Journal
LA English
AB The cannabimimetic activity of two enantiomeric pairs of compds. structurally different from the classical cannabinoids was evaluated in rats and pigeons, trained to discriminate between the presence and absence of (-)-.DELTA.-9-tetrahydrocannabinol (THC). One pair of enantiomers [compds. (+)-HU-249 and (-)-HU-250] has a 5-membered oxygen-contg. benzofuran ring; the second pair [(+)-HU-253 and (-)-HU-254] does not have an oxygen-contg. ring. The onset of cannabimimetic activity was slower, and duration of action was longer for the test compds. than for THC. HU-250 exhibited cannabimimetic activity with a potency similar to THC in both species; HU-249 was 22 times less active than THC. The pattern of response rate and THC-like responding obtained with HU-249 were dissocd.; THC-like responding occurred during the later test intervals when suppression of response rate was reduced. HU-250 bound to the cannabinoid receptor with a Ki of 47.6 nM, essentially identical to that of THC. HU-249 was much less active, with a Ki of 28.3 .mu.M. The triacetate enantiomers, HU-253 and HU-254, occasioned THC-like responding in both species, HU-254 being about 4.5 times less potent than THC and 3 to 4 times more potent than HU-253. In binding, HU-253 was also less potent than HU-254. The corresponding triols were considerably more potent than the acetates; (-)-HU-256 had a Ki of 198 nM, whereas (+)-HU-255 had a Ki of 43.8 nM, comparable to that of THC.
IT **76163-87-6**, HU 254 **76163-88-7**, HU 253
RL: BIOL (Biological study)
(cannabinoid receptor binding and tetrahydrocannibinol discriminative stimulus effect response to, structure in relation to)
RN 76163-87-6 CAPLUS
CN 1,3-Benzenediol, 2-[4-[(acetyloxy)methyl]-6,6-dimethylbicyclo[3.1.1]hept-3-en-2-yl]-5-(1,1-dimethylheptyl)-, diacetate, [1S-

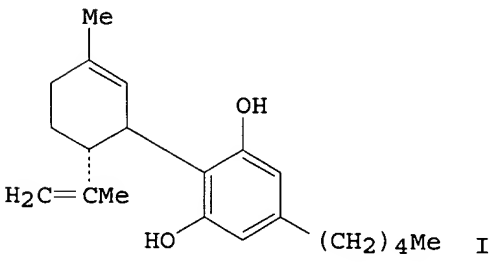
(1.alpha.,2.alpha.,5.alpha.)]- (9CI) (CA INDEX NAME)



RN 76163-88-7 CAPLUS
CN 1,3-Benzenediol, 2-[4-[(acetyloxy)methyl]-6,6-dimethylbicyclo[3.1.1]hept-3-en-2-yl]-5-(1,1-dimethylheptyl)-, diacetate, [1R-(1.alpha.,2.alpha.,5.alpha.)]- (9CI) (CA INDEX NAME)



L7 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2002 ACS
AN 1988:142840 CAPLUS
DN 108:142840
TI Structure-anticonvulsant activity relationships of cannabidiol analogs
AU Martin, Arnold R.; Consroe, Paul; Kane, Vinayak V.; Shah, Vibhakar; Singh, Vishwakarma; Lander, Naftali; Mechoulam, Raphael; Srebnik, Morris
CS Coll. Pharm., Univ. Arizona, Tucson, AZ, 85721, USA
SO NIDA Res. Monogr. (1987), 79(Struct.-Act. Relat. Cannabinoids), 48-58
CODEN: MIDAD4; ISSN: 0361-8595
DT Journal
LA English
GI

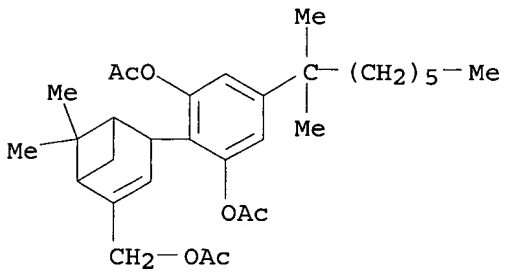


AB Cannabidiol (I) exhibits anticonvulsant activity in exptl. animals and in man. As part of a structure-activity study, analogs were prepd. wherein

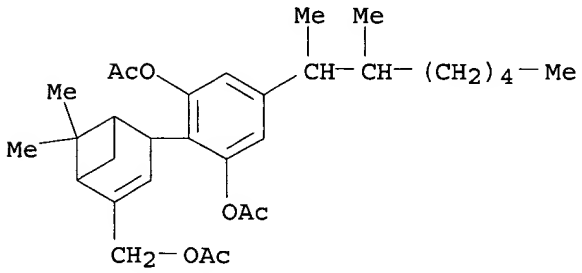
the terpene unit, the aryl unit, and/or the side chain were modified. Thus, several pinenyl and carenyl derivs., aryl ethers and acetates, and a variety of 1'',1''-dialkylhexyl and 1'',1''-dialkylheptyl analogs were synthesized. The compds. were evaluated for anticonvulsant activity in seizure-susceptible rats and for neurotoxicity in the rat rotorod test. Comparisons of stereoisomers of I and several analogs revealed a general lack of stereoselectivity for anticonvulsant and other central nervous system-affecting properties of this class of compds.

IT **76163-87-6P 76163-89-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and anticonvulsant activity-structure relations of)

RN 76163-87-6 CAPLUS
CN 1,3-Benzenediol, 2-[4-[(acetyloxy)methyl]-6,6-dimethylbicyclo[3.1.1]hept-3-en-2-yl]-5-(1,1-dimethylheptyl)-, diacetate, [1S-(1.alpha.,2.alpha.,5.alpha.)]- (9CI) (CA INDEX NAME)



RN 76163-89-8 CAPLUS
CN 1,3-Benzenediol, 2-[4-[(acetyloxy)methyl]-6,6-dimethylbicyclo[3.1.1]hept-3-en-2-yl]-5-(1,2-dimethylheptyl)-, diacetate (9CI) (CA INDEX NAME)

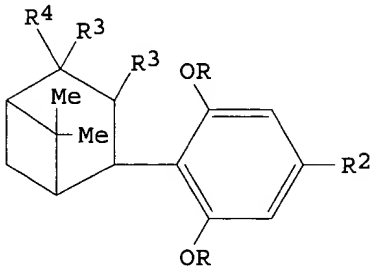


L7 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2002 ACS
AN 1981:480289 CAPLUS
DN 95:80289
TI Pinene derivatives, their preparation and pharmaceutical compositions comprising them
IN Mechaulam, Raphael; Lander, Naftali; Dikstein, Shabtay
PA Yissum Research and Development Co., Israel; Plantex Ltd.
SO Brit. UK Pat. Appl., 7 pp.
CODEN: BAXXDU
DT Patent
LA English
FAN.CNT 1

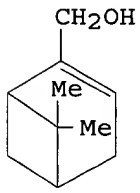
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI GB 2027021	A	19800213	GB 1979-25214	19790719

	GB 2027021	B2	19830427		
	IL 55274	A1	19820831	IL 1978-55274	19780802
	DE 2929517	A1	19800221	DE 1979-2929517	19790720
	US 4282248	A	19810804	US 1979-59859	19790723
	FR 2432498	A1	19800229	FR 1979-19764	19790801
	FR 2432498	B1	19840921		
PRAI	IL 1978-55274		19780802		

GI



I



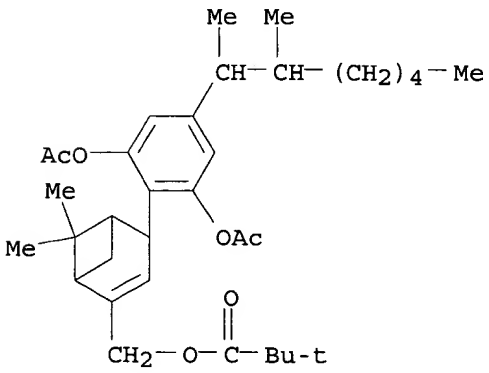
II

AB Pinene derivs. I [R = H, COR1 (R1 = C1-5 alkyl); R2 = Me(CH2)5CMe2, Me(CH2)4CHMeCHMe; R3 = H, R4 = Me; R32 = bond, R4 = CH2OH, CH2OR5 (R5 = C1-5 alkyl)] were prepd. E.g., myrtenol (II) underwent sequential esterification with Me3CCOCl, oxidn. (Na2Cr2O7), redn. [LiAlH(OCMe3)3], reaction with 5-(1,2-dimethylheptyl)resorcinol, and acetylation to give I [R = Ac, R2 = Me(CH2)4CHMeCHMe, R32 = bond, R4 = CH2O2CCMe3] (III). I are useful as analgesics; their activity was assessed by the mouse ring and tail-flick methods and by the rat foot-pressure method. ED50 values for III were 25, >50, and >50 mg/kg, resp. I are also of value as central-nervous-system depressants, sedatives, tranquilizers, anticonvulsants, antimigraine agents, antiglaucoma agents, antidiarrheal agents, antiinflammatory agents, antinausea agents, and antiulcer agents.

IT **76163-92-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and analgesic properties of)

RN 76163-92-3 CAPLUS

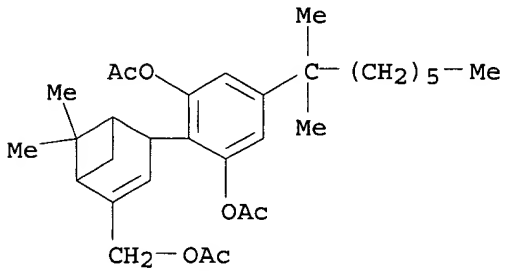
CN Propanoic acid, 2,2-dimethyl-, [4-[2,6-bis(acetyloxy)-4-(1,2-dimethylheptyl)phenyl]-6,6-dimethylbicyclo[3.1.1]hept-2-en-2-yl]methyl ester (9CI) (CA INDEX NAME)



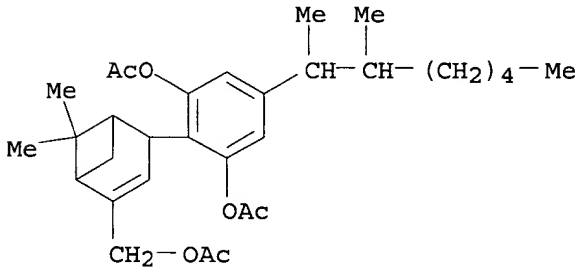
IT **76163-88-7P 76163-89-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn., analgesic properties, and redn. of)

CAS ONLINE PRINTOUT 09/698,071

RN 76163-88-7 CAPLUS
CN 1,3-Benzenediol, 2-[4-[(acetyloxy)methyl]-6,6-dimethylbicyclo[3.1.1]hept-3-en-2-yl]-5-(1,1-dimethylheptyl)-, diacetate, [1R-(1.alpha.,2.alpha.,5.alpha.)]- (9CI) (CA INDEX NAME)



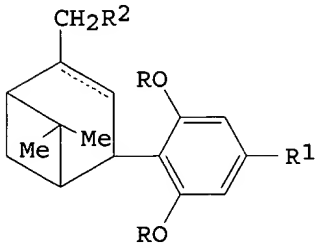
RN 76163-89-8 CAPLUS
CN 1,3-Benzenediol, 2-[4-[(acetyloxy)methyl]-6,6-dimethylbicyclo[3.1.1]hept-3-en-2-yl]-5-(1,2-dimethylheptyl)-, diacetate (9CI) (CA INDEX NAME)



L7 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2002 ACS
AN 1981:47552 CAPLUS
DN 94:47552
TI Phenylpinene derivatives, their preparation and pharmaceutical compositions comprising them
IN Mechoulam, Raphael; Lander, Naftali; Dikstein, Shabtay
PA Yissum Research and Development Co., Israel
SO Brit. UK Pat. Appl., 7 pp.
CODEN: BAXXDU
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	GB 2027021		19800213		
PRAI	IL 1978-55274		19780802		

GI



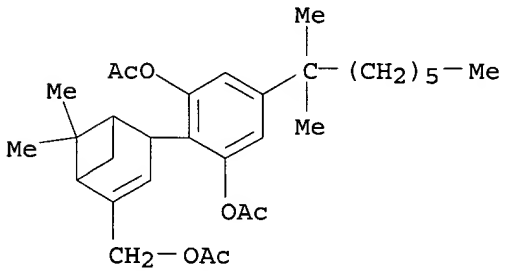
I

AB The prepn. of the title compds. I (R = H, C2-6 alkanoyl; R1 = 1,1- or 1,2-dimethylheptyl; R2 = H, OH, C1-5 acyloxy) is described. Thus, (-)-I (R = Ac, R1 = 1,2-dimethylheptyl, R2 = O2CCMe3, double bond present) was prepd. from (-)-myrtenol by sequential treatment with Me3CCOCl, Na2Cr2O4, LiAlH(OCMe3)3, 5-(1,2-dimethylheptyl)resorcinol/p-MeC6H4SO3H, and Ac2O. I have analgesic, sedative, tranquilizing, central nervous system depressant, anticonvulsive, antimigraine, antiglaucoma, antinausea, antiulcer, antidiarrheal, and antiinflammatory activity. The analgesic activities of I (reported) were assessed in mice by the AcOH-induced writhing test and the tail flick test, and in rats by the foot pressure test. The central nervous system action (not reported) was tested by the mouse ring test.

IT **76163-87-6P 76163-88-7P 76163-89-8P**
76163-90-1P 76163-91-2P 76163-92-3P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and analgesic activity of)

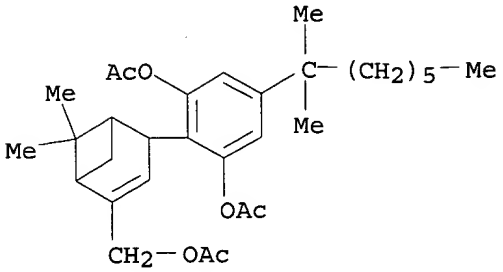
RN 76163-87-6 CAPLUS

CN 1,3-Benzenediol, 2-[4-[(acetyloxy)methyl]-6,6-dimethylbicyclo[3.1.1]hept-3-en-2-yl]-5-(1,1-dimethylheptyl)-, diacetate, [1S-(1.alpha.,2.alpha.,5.alpha.)]- (9CI) (CA INDEX NAME)

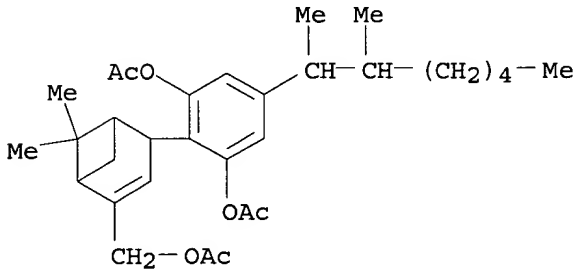


RN 76163-88-7 CAPLUS

CN 1,3-Benzenediol, 2-[4-[(acetyloxy)methyl]-6,6-dimethylbicyclo[3.1.1]hept-3-en-2-yl]-5-(1,1-dimethylheptyl)-, diacetate, [1R-(1.alpha.,2.alpha.,5.alpha.)]- (9CI) (CA INDEX NAME)

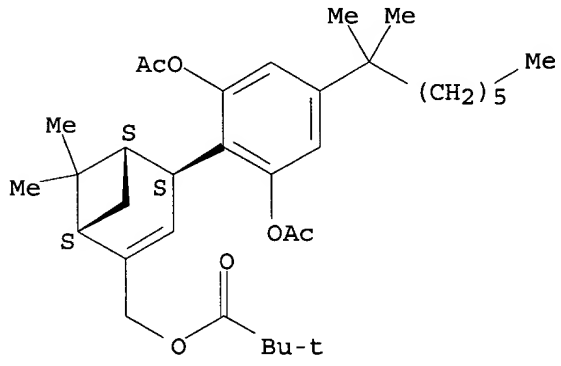


RN 76163-89-8 CAPLUS
CN 1,3-Benzenediol, 2-[4-[(acetyloxy)methyl]-6,6-dimethylbicyclo[3.1.1]hept-3-en-2-yl]-5-(1,2-dimethylheptyl)-, diacetate (9CI) (CA INDEX NAME)



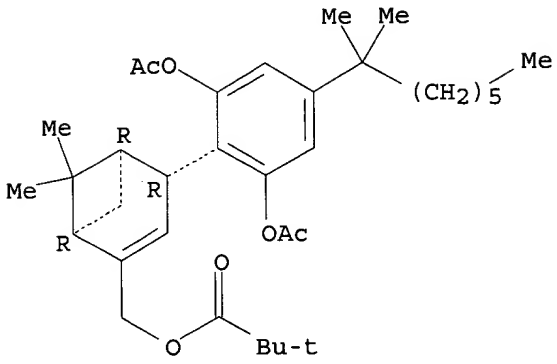
RN 76163-90-1 CAPLUS
CN Propanoic acid, 2,2-dimethyl-, [4-[2,6-bis(acetyloxy)-4-(1,1-dimethylheptyl)phenyl]-6,6-dimethylbicyclo[3.1.1]hept-2-en-2-yl]methyl ester, [1S-(1.alpha.,4.alpha.,5.alpha.)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

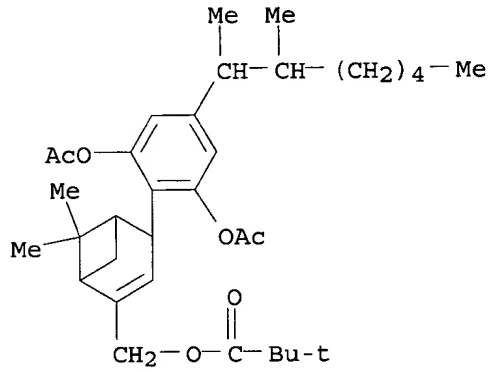


RN 76163-91-2 CAPLUS
CN Propanoic acid, 2,2-dimethyl-, [4-[2,6-bis(acetyloxy)-4-(1,1-dimethylheptyl)phenyl]-6,6-dimethylbicyclo[3.1.1]hept-2-en-2-yl]methyl ester, [1R-(1.alpha.,4.alpha.,5.alpha.)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 76163-92-3 CAPLUS
CN Propanoic acid, 2,2-dimethyl-, [4-[2,6-bis(acetyloxy)-4-(1,2-dimethylheptyl)phenyl]-6,6-dimethylbicyclo[3.1.1]hept-2-en-2-yl]methyl ester (9CI) (CA INDEX NAME)



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